

L4 ANSWER 1 OF 4 MEDLINE on STN  
 AN 2003314113 IN-PROCESS  
 DN 22726392 PubMed ID: 12842017  
 TI **TRPM5** is a voltage-modulated and Ca(2+)-activated monovalent selective cation channel.  
 AU Hofmann Thomas; Chubanov Vladimir; Gudermann Thomas; Montell Craig  
 CS Department of Biological Chemistry, Johns Hopkins University School of Medicine, 725 North Wolfe Street, Baltimore, MD 21215, USA.  
 NC EY10852 (NEI)  
 SO CURRENT BIOLOGY, (2003 Jul 1) 13 (13) 1153-8.  
 Journal code: 9107782. ISSN: 0960-9822.  
 CY England: United Kingdom  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS IN-PROCESS; NONINDEXED; Priority Journals  
 ED Entered STN: 20030708  
 Last Updated on STN: 20030723  
 AB The **TRPM** subfamily of mammalian **TRP** channels displays unusually diverse activation mechanisms and selectivities. One member of this subfamily, **TRPM5**, functions in **taste receptor** cells and has been reported to be activated through G protein-coupled receptors linked to phospholipase C. However, the specific mechanisms regulating **TRPM5** have not been described. Here, we demonstrate that **TRPM5** is a monovalent-specific cation channel with a 23 pS unitary conductance. **TRPM5** does not display constitutive activity. Rather, it is activated by stimulation of a receptor pathway coupled to phospholipase C and by IP(3)-mediated Ca(2+) release. Gating of **TRPM5** was dependent on a rise in Ca(2+) because it was fully activated by Ca(2+). Unlike any previously described mammalian **TRP** channel, **TRPM5** displayed voltage modulation and rapid activation and deactivation kinetics upon receptor stimulation. The most closely related protein, the Ca(2+)-activated monovalent-selective cation channel **TRPM4b**, also showed voltage modulation, although with slower relaxation kinetics than **TRPM5**. Taken together, the data demonstrate that **TRPM5** and **TRPM4b** represent the first examples of voltage-modulated, Ca(2+)-activated, monovalent cation channels (VCAMs). The voltage modulation and rapid kinetics provide **TRPM5** with an excellent set of properties for participating in signaling in **taste receptors** and other excitable cells.

L4 ANSWER 2 OF 4 MEDLINE on STN  
 AN 2003243452 IN-PROCESS  
 DN 22650589 PubMed ID: 12765699  
 TI Making sense with **TRP** channels: store-operated calcium entry and the ion channel **Trpm5** in **taste receptor** cells.  
 AU Perez Cristian A; Margolskee Robert F; Kinnamon Sue C; Ogura Tatsuya  
 CS Department of Physiology & Biophysics, Howard Hughes Medical Institute, Mount Sinai School of Medicine, New York University, New York, NY 10029, USA.. Cristian.Perez@rockefeller.edu  
 NC DC 00766 (NIDCD)  
 DC 03055 (NIDCD)  
 DC 03155 (NIDCD)  
 DC 05140 (NIDCD)  
 SO CELL CALCIUM, (2003 May-Jun) 33 (5-6) 541-9.  
 Journal code: 8006226. ISSN: 0143-4160.  
 CY Scotland: United Kingdom  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS IN-PROCESS; NONINDEXED; Priority Journals  
 ED Entered STN: 20030528

Last Updated on STN: 20030719

AB The sense of taste plays a critical role in the life and nutritional status of organisms. During the last decade, several molecules involved in taste detection and transduction have been identified, providing a better understanding of the molecular physiology of **taste receptor** cells. However, a comprehensive catalogue of the **taste receptor** cell signaling machinery is still unavailable. We have recently described the occurrence of calcium signaling mechanisms in **taste receptor** cells via apparent store-operated channels and identified **Trpm5**, a novel candidate taste transduction element belonging to the mammalian family of transient receptor potential channels. **Trpm5** is expressed in a tissue-restricted manner, with high levels in gustatory tissue. In taste cells, **Trpm5** is co-expressed with taste-signaling molecules such as alpha-gustducin, Ggamma(13), phospholipase C beta(2) and inositol 1,4,5-trisphosphate receptor type III. Biophysical studies of **Trpm5** heterologously expressed in *Xenopus* oocytes and mammalian CHO-K1 cells indicate that it functions as a store-operated channel that mediates capacitative calcium entry. The role of store-operated channels and **Trpm5** in capacitative calcium entry in **taste receptor** cells in response to bitter compounds is discussed.

L4 ANSWER 3 OF 4 MEDLINE on STN

AN 2003071120 MEDLINE

DN 22469025 PubMed ID: 12581520

TI Coding of sweet, bitter, and umami tastes: different receptor cells sharing similar signaling pathways.

CM Comment on: Cell. 2003 Feb 7;112(3):283-4

AU Zhang Yifeng; Hoon Mark A; Chandrashekar Jayaram; Mueller Ken L; Cook Boaz; Wu Dianqing; Zuker Charles S; Ryba Nicholas J P

CS Howard Hughes Medical Institute, Department of Biology, University of California, San Diego, La Jolla, CA 92093, USA.

SO CELL, (2003 Feb 7) 112 (3) 293-301.

Journal code: 0413066. ISSN: 0092-8674.

CY United States

DT Commentary

Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200303

ED Entered STN: 20030214

Last Updated on STN: 20030319

Entered Medline: 20030318

AB Mammals can taste a wide repertoire of chemosensory stimuli. Two unrelated families of receptors (T1Rs and T2Rs) mediate responses to sweet, amino acids, and bitter compounds. Here, we demonstrate that knockouts of **TRPM5**, a taste **TRP** ion channel, or **PLCbeta2**, a phospholipase C selectively expressed in taste tissue, abolish sweet, amino acid, and bitter taste reception, but do not impact sour or salty tastes. Therefore, despite relying on different receptors, sweet, amino acid, and bitter transduction converge on common signaling molecules. Using **PLCbeta2** taste-blind animals, we then examined a fundamental question in taste perception: how taste modalities are encoded at the cellular level. Mice engineered to rescue **PLCbeta2** function exclusively in bitter-receptor expressing cells respond normally to bitter tastants but do not taste sweet or amino acid stimuli. Thus, bitter is encoded independently of sweet and amino acids, and **taste receptor** cells are not broadly tuned across these modalities.

L4 ANSWER 4 OF 4 MEDLINE on STN

AN 2002667923 MEDLINE

DN 22292154 PubMed ID: 12368808

TI A transient receptor potential channel expressed in **taste receptor** cells.  
 AU Perez Cristian A; Huang Liquan; Rong Mingqing; Kozak J Ashot; Preuss Axel K; Zhang Hailin; Max Marianna; Margolskee Robert F  
 CS Howard Hughes Medical Institute, Mount Sinai School of Medicine, New York University, Box 1677, 1425 Madison Avenue, New York, New York 10029, USA.  
 NC DC00310 (NIDCD)  
 DC03055 (NIDCD)  
 DC03155 (NIDCD)  
 SO NATURE NEUROSCIENCE, (2002 Nov) 5 (11) 1169-76.  
 Journal code: 9809671. ISSN: 1097-6256.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 200212  
 ED Entered STN: 20021114  
 Last Updated on STN: 20021217  
 Entered Medline: 20021205  
 AB We used differential screening of cDNAs from individual **taste receptor** cells to identify candidate taste transduction elements in mice. Among the differentially expressed clones, one encoded **Trpm5**, a member of the mammalian family of transient receptor potential (TRP) channels. We found **Trpm5** to be expressed in a restricted manner, with particularly high levels in taste tissue. In taste cells, **Trpm5** was coexpressed with taste-signaling molecules such as alpha-gustducin, Ggamma13, phospholipase C-beta2 (PLC-beta2) and inositol 1,4,5-trisphosphate receptor type III (IP3R3). Our heterologous expression studies of **Trpm5** indicate that it functions as a cationic channel that is gated when internal calcium stores are depleted. **Trpm5** may be responsible for capacitative calcium entry in **taste receptor** cells that respond to bitter and/or sweet compounds.

L2 ANSWER 1 OF 1 MEDLINE on STN  
 AN 2001504152 MEDLINE  
 DN 21438010 PubMed ID: 11535825  
 TI **Regulation of melastatin**, a TRP-related protein,  
 through interaction with a cytoplasmic isoform.  
 AU Xu X Z; Moebius F; Gill D L; Montell C  
 CS Department of Biological Chemistry, The Johns Hopkins University School of  
 Medicine, Baltimore, MD 21205, USA.  
 NC EY10852 (NEI)  
 SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF  
 AMERICA, (2001 Sep 11) 98 (19) 10692-7.  
 Journal code: 7505876. ISSN: 0027-8424.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 OS GENBANK-AY046396  
 EM 200111  
 ED Entered STN: 20010913  
 Last Updated on STN: 20030105  
 Entered Medline: 20011101  
 AB The TRP (transient receptor potential) superfamily includes a group of  
 subfamilies of channel-like proteins mediating a multitude of  
 physiological signaling processes. The TRP-melastatin (TRPM) subfamily  
 includes the putative tumor suppressor melastatin (MLSN) and is a poorly  
 characterized group of TRP-related proteins. Here, we describe the  
 identification and characterization of an additional TRPM protein TRPM4.  
 We reveal that TRPM4 and MLSN each mediate Ca(2+) entry when expressed in  
 HEK293 cells. Furthermore, we demonstrate that a short form of MLSN  
 (MLSN-S) interacts directly with and suppresses the activity of  
 full-length MLSN (MLSN-L). This suppression seems to result from the  
 inhibition of translocation of MLSN-L to the plasma membrane. We propose  
 that control of translocation through interaction between MLSN-S and  
 MLSN-L represents a mode for regulating ion channel activity.

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YOU HAVE REQUESTED DATA FROM 19 ANSWERS - CONTINUE? Y/(N):y

L1 ANSWER 1 OF 19 MEDLINE on STN  
 AN 2003401923 MEDLINE  
 DN 22821189 PubMed ID: 12940649  
 TI Diffuse neuroaxonal involvement in mucopolipidosis IV as assessed by proton  
 magnetic resonance spectroscopic imaging.  
 AU Bonavita Simona; Virta Anette; Jeffries Neal; Goldin Ehud; Tedeschi  
 Gioacchino; Schiffmann Raphael  
 CS Second Division of Neurology, Second University of Naples, Italy.  
 SO JOURNAL OF CHILD NEUROLOGY, (2003 Jul) 18 (7) 443-9.  
 Journal code: 8606714. ISSN: 0883-0738.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 200309  
 ED Entered STN: 20030828  
 Last Updated on STN: 20030910  
 Entered Medline: 20030909  
 AB Mucopolipidosis IV is an autosomal recessive disorder caused by mutations in  
 MCOLN1, which codes for mucolipin, a **transient receptor  
 potential protein**. In order to investigate brain  
 metabolic abnormalities in mucopolipidosis IV, we studied 14 patients (11

children, 3 adults) by proton magnetic resonance spectroscopic imaging. The ratios of N-acetylaspartate/ creatine-phosphocreatine and N-acetylaspartate/choline-containing compounds in patients with mucopolipidosis IV were significantly reduced in all regions of interest except the parietal gray matter and thalamus. The ratios of choline-containing compounds/creatine-phosphocreatine was not significantly reduced in patients compared with controls. The ratio of N-acetylaspartate/creatine-phosphocreatine were significantly lower ( $P = .005$ ) in the more neurologically impaired patients compared with the least impaired. For every region of interest, except for parietal gray matter, the ratio of N-acetylaspartate/creatine-phosphocreatine was lower in the more motorically impaired patient group. There was no difference for the ratio of N-acetylaspartate/creatine-phosphocreatine between younger and older patients. These findings suggest that mucopolipidosis IV is largely a static developmental encephalopathy associated with diffuse neuronal and axonal damage or dysfunction. Mucolin deficiency impairs motor more than sensory central nervous system pathways.

L1 ANSWER 2 OF 19 MEDLINE on STN  
 AN 2003326844 MEDLINE  
 DN 22740393 PubMed ID: 12856738  
 TI Evidence for the expression of **transient receptor potential proteins** in guinea pig airway smooth muscle cells.  
 AU Ong Hwei L; Brereton Helen M; Harland M Lyn; Barritt Greg J  
 CS Department of Medical Biochemistry, School of Medicine, Flinders University, Adelaide, South Australia, Australia.  
 SO RESPIROLOGY, (2003 Mar) 8 (1) 23-32.  
 Journal code: 9616368. ISSN: 1323-7799.  
 CY Australia  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 200308  
 ED Entered STN: 20030715  
 Last Updated on STN: 20030815  
 Entered Medline: 20030814  
 AB OBJECTIVE: The present study investigates the expression of transient receptor potential (TRPC) proteins in airway smooth muscle (ASM) cells in order to determine whether these proteins may be candidate molecular counterparts of plasma membrane  $\text{Ca}^{2+}$ -permeable channels involved in the contraction of ASM. METHODS: Expression of TRPC mRNA was detected using specific primers and RT-PCR. Expression of the TRPC1, TRPC3 and TRPC6 proteins was detected using antibodies in immunoprecipitation and Western blot. RESULTS: Guinea pig ASM cells exhibited thapsigargin- and acetylcholine-initiated  $\text{Ca}^{2+}$  inflow but none by 1-oleoyl-2-acetyl-sn-glycerol. mRNA encoding each of the TRPC1 to TRPC6 proteins was detected in ASM cells. mRNA encoding TRPC1, TRPC3, TRPC4 and TRPC6 was detected in ASM cells at a concentration approximately equivalent to that in guinea pig brain. mRNA encoding TRPC2 and TRPC5 was more abundant in ASM cells than in brain. The TRPC1 protein, but not the TRPC3 or TRPC6 proteins, was detected in extracts of ASM cells, while all three proteins were detected in brain. CONCLUSION: The results provide evidence for a low level of expression of the TRPC1 to TRPC6 proteins in ASM cells. These proteins may function as store-operated  $\text{Ca}^{2+}$  and/or second messenger-activated non-selective cation channels in ASM cells.

L1 ANSWER 3 OF 19 MEDLINE on STN  
 AN 2003199843 IN-PROCESS  
 DN 22605411 PubMed ID: 12719655  
 TI **Transient receptor potential protein**  
 as a novel non-voltage-gated  $\text{Ca}^{2+}$  entry channel involved in diverse

pathophysiological functions.

AU Inoue Ryuji; Hanano Toyohisa; Shi Juan; Mori Yasuo; Ito Yushi  
CS Department of Pharmacology, Graduate School of Medical Sciences, Kyushu University, Fukuoka 812-8582, Japan.. inouery@pharmaco.med.kyushu-u.ac.jp  
SO J Pharmacol Sci, (2003 Apr) 91 (4) 271-6.  
Journal code: 101167001. ISSN: 1347-8613.  
CY Japan  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS IN-PROCESS; NONINDEXED; Priority Journals  
ED Entered STN: 20030430  
Last Updated on STN: 20030730  
AB In both excitable and non-excitable cells, many chemical and physical stimuli elicit continuous Ca<sup>2+</sup> influx through yet poorly understood pathways distinct from voltage-gated Ca<sup>2+</sup> channels, leading to activation and modulation of various cellular functions. The molecular entities of these pathways have long been enigmatic, but important clues have been obtained from recent investigations on the Drosophila transient receptor potential (TRP) protein and its mammalian homologues. TRP proteins function as non-voltage-gated Ca<sup>2+</sup> channels that are constitutively active or gated by a multitude of stimuli including light, pheromones, lipids, temperature, acid, osmolarity, and oxidative stress; and thus they may play divergent roles in cell pathophysiology. This short paper briefly overviews the current knowledge about these channels with a main focus on their possible linkage with in vivo function.

L1 ANSWER 4 OF 19 MEDLINE on STN  
AN 2002622933 MEDLINE  
DN 22268128 PubMed ID: 12381092  
TI Cloning and functional expression of a novel splice variant of rat TRPC4.  
AU Satoh Eisaku; Ono Kyoichi; Xu Feng; Iijima Toshihiko  
CS Department of Pharmacology, Akita University School of Medicine, Japan.  
SO Circ J, (2002 Oct) 66 (10) 954-8.  
Journal code: 101137683. ISSN: 1346-9843.  
CY Japan  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200306  
ED Entered STN: 20021017  
Last Updated on STN: 20030606  
Entered Medline: 20030605

AB **Transient receptor potential protein**  
4 (TRPC4) has been identified as a candidate for the capacitative calcium entry (CCE) channels, but its functional role is still controversial. Using a RT-PCR technique, a novel isoform of TRPC4, designated rTRPC4gamma, was isolated. It was nearly identical to full-length rTRPC4 (rTRPC4alpha), except that it lacked 53 nucleotides that correspond to the predicted linker between the second and third transmembrane domain of rTRPC4alpha, and its mRNA was expressed in brain and heart. This splice variant encoded a potential protein of 400 residues that consists of an amino-terminal cytoplasmic domain and 2 transmembrane domains by a frameshift mutation. When rTRPC4gamma cDNA was transiently transfected to HEK-293 cells, thapsigargin (TG)-induced Ca<sup>2+</sup> entry was suppressed significantly. By contrast, expression of rTRPC4 did not affect TG-induced Ca<sup>2+</sup> entry. To investigate the subcellular localization, plasmids were constructed with green fluorescence protein (GFP) as an amino-terminal fusion to rTRPC4 variants. GFP-rTRPC4gamma fusion protein, unlike GFP-rTRPC4alpha, was localized to the cytoplasm as well as plasma membrane. These results suggest that rTRPC4gamma may play a modulatory role in CCE channel activity in the brain and heart.

L1 ANSWER 5 OF 19 MEDLINE on STN  
 AN 2002378363 MEDLINE  
 DN 22119696 PubMed ID: 12123831  
 TI Structural domains required for channel function of the mouse  
**transient receptor potential protein**  
 homologue TRP1beta.  
 AU Engelke Michael; Friedrich Olaf; Budde Petra; Schafer Christina; Niemann  
 Ursula; Zitt Christof; Jungling Eberhard; Rocks Oliver; Luckhoff Andreas;  
 Frey Jurgen  
 CS Universitat Bielefeld, Fakultat fur Chemie, Biochemie II,  
 Universitatsstrasse 25, D-33615, Bielefeld, Germany.  
 SO FEBS LETTERS, (2002 Jul 17) 523 (1-3) 193-9.  
 Journal code: 0155157. ISSN: 0014-5793.  
 CY Netherlands  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 200209  
 ED Entered STN: 20020719  
 Last Updated on STN: 20020918  
 Entered Medline: 20020917  
 AB **Transient receptor potential**  
**proteins** (TRP) are supposed to participate in the formation of  
 store-operated Ca(2+) influx channels by co-assembly. However, little is  
 known which domains facilitate the interaction of subunits. Contribution  
 of the N-terminal coiled-coil domain and ankyrin-like repeats and the  
 putative pore region of the mouse TRP1beta (mTRP1beta) variant to the  
 formation of functional cation channels were analyzed following  
 overexpression in HEK293 (human embryonic kidney) cells. MTRP1beta  
 expressing cells exhibited enhanced Ca(2+) influx and enhanced whole-cell  
 membrane currents compared to mTRP1beta deletion mutants. Using a yeast  
 two-hybrid assay only the coiled-coil domain facilitated homodimerization  
 of the N-terminus. These results suggest that the N-terminus of mTRP1beta  
 is required for structural organization thus forming functional channels.

L1 ANSWER 6 OF 19 MEDLINE on STN  
 AN 2002289955 MEDLINE  
 DN 22026120 PubMed ID: 12030534  
 TI Receptor-operated Ca2(+)-permeable nonselective cation channels in  
 vascular smooth muscle: a physiologic perspective.  
 AU Large William A  
 CS Department of Pharmacology and Clinical Pharmacology, St. George's  
 Hospital Medical School, London, United Kingdom.. w.large@sghms.ac.uk  
 SO JOURNAL OF CARDIOVASCULAR ELECTROPHYSIOLOGY, (2002 May) 13 (5) 493-501.  
 Ref: 48  
 Journal code: 9010756. ISSN: 1045-3873.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 LA English  
 FS Priority Journals  
 EM 200210  
 ED Entered STN: 20020528  
 Last Updated on STN: 20021019  
 Entered Medline: 20021018  
 AB This article summarizes the literature on receptor-operated  
 Ca2(+)-permeable nonselective cation channels in vascular smooth muscle  
 cells. One of these conductances, the P2X1 receptor, is a classic  
 ligand-gated channel, but others are likely to be mediated via  
 G-protein-coupled receptors. The most studied receptor-operated channel  
 in vascular myocytes is the norepinephrine-evoked nonselective cation

channel in rabbit portal vein myocytes. The data regarding the transduction mechanisms and biophysical properties of whole-cell and single-channel currents in this preparation are described. The channels have a conductance of 20 to 25 pS and complex kinetic behavior with at least two open and two closed states. These channels are activated by norepinephrine and acetylcholine via G-protein-coupled receptors linked to phospholipase C and by diacylglycerol (DAG). The action of DAG occurs by a mechanism independent of protein kinase C, but other kinases may mediate the responses to norepinephrine and DAG. In addition, activation of tyrosine kinases leads to opening of this channel. Other vasoconstrictors, such as endothelin, vasopressin, serotonin, and angiotensin II, open  $\text{Ca}^{2+}$ -permeable nonselective cation channels, but there may be differences between these conductances and the norepinephrine-evoked channels. A homologue of the **transient receptor potential protein** (TRPC6) is an essential component of the norepinephrine-activated channel in rabbit portal vein, and it is likely that this family of proteins plays an important role in mediating  $\text{Ca}^{2+}$  influx in vascular smooth muscle.

L1 ANSWER 7 OF 19 MEDLINE on STN  
 AN 2002082041 MEDLINE  
 DN 21667496 PubMed ID: 11808331  
 TI The TRP proteins, a rapidly expanding  $\text{Ca}^{2+}$  entry channel family and a new molecular target for drug development.  
 AU Inoue Ryuji; Ito Yushi; Mori Yasuo  
 CS Department of Pharmacology, Graduate School of Medical Science, Kyushu University.  
 SO NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, (2002 Jan) 60 (1) 18-24. Ref: 21  
 Journal code: 0420546. ISSN: 0047-1852.  
 CY Japan  
 DT Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 LA Japanese  
 FS Priority Journals  
 EM 200202  
 ED Entered STN: 20020128  
 Last Updated on STN: 20020227  
 Entered Medline: 20020226  
 AB There is a rapidly expanding protein family which encompasses a broad repertoire of cation-selective channels serving as a continuous  $\text{Ca}^{2+}$  entry pathway into the cell. The **transient receptor potential protein** (TRP) and its relatives, which were originally thought to be  $\text{Ca}^{2+}$ -permeable cation channels activated upon the stimulation of G-protein coupled and tyrosine kinase receptors, are now becoming promising candidates mediating a variety of cellular responses and functions such as mechano/chemo-transduction, oxidative stress, and cell survival/proliferation. This short paper briefly overviews the current knowledge about these proteins as a new target for drug discovery and development.

L1 ANSWER 8 OF 19 MEDLINE on STN  
 AN 2001492758 MEDLINE  
 DN 21426412 PubMed ID: 11535132  
 TI A diacylglycerol-activated  $\text{Ca}^{2+}$  channel in PC12 cells (an adrenal chromaffin cell line) correlates with expression of the TRP-6 (**transient receptor potential**) protein  
 .  
 AU Tesfai Y; Brereton H M; Barritt G J  
 CS Department of Medical Biochemistry, School of Medicine, Faculty of Health Sciences, Flinders University, G.P.O. Box 2100, Adelaide, South Australia,



5001, Australia.

SO BIOCHEMICAL JOURNAL, (2001 Sep 15) 358 (Pt 3) 717-26.  
Journal code: 2984726R. ISSN: 0264-6021.

CY England: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200110

ED Entered STN: 20010906  
Last Updated on STN: 20011029  
Entered Medline: 20011025

AB The structures, and mechanisms of activation, of plasma membrane intracellular-messenger-activated, non-selective cation channels in animal cells are not well understood. The PC12 adrenal chromaffin cell line is a well-characterized example of a nerve cell. In PC12 cells, 1-oleoyl-2-acetyl-sn-glycerol (OAG), a membrane-permeant analogue of diacylglycerol, initiated the inflow of  $\text{Ca}^{2+}$ ,  $\text{Mn}^{2+}$  and  $\text{Sr}^{2+}$ . Acetylcholine and thapsigargin initiated the inflow of  $\text{Ca}^{2+}$  and  $\text{Mn}^{2+}$ , but not of  $\text{Sr}^{2+}$ . The activation of bivalent cation inflow by OAG: (i) was mimicked by another membrane-permeant diacylglycerol analogue, 1,2-dioctanoyl-sn-glycerol, but not by the membrane-impermeant analogue 1-stearoyl-2-arachidonyl-sn-glycerol; (ii) was not blocked by staurosporin or chelerythrine, inhibitors of protein kinase C; (iii) was enhanced by RHC80267 and R50922, inhibitors of diacylglycerol lipase and diacylglycerol kinase respectively; and (iv) was inhibited by extracellular  $\text{Ca}^{2+}$ . When OAG was added after acetylcholine, the effect of OAG on  $\text{Ca}^{2+}$  inflow was over-and-above that induced by acetylcholine. 2-Aminoethyl diphenylborate (2-APB) inhibited  $\text{Ca}^{2+}$  inflow initiated by either acetylcholine or thapsigargin, but not that initiated by OAG. Flufenamic acid inhibited OAG-initiated, but not acetylcholine-initiated,  $\text{Ca}^{2+}$  and  $\text{Mn}^{2+}$  inflow. OAG-initiated  $\text{Ca}^{2+}$  inflow was less sensitive to inhibition by SK&F96365 than acetylcholine-initiated  $\text{Ca}^{2+}$  inflow. In polyadenylated RNA prepared from PC12 cells, mRNA encoding TRP (**transient receptor potential**) proteins 1-6 was detected by reverse transcriptase (RT)-PCR, and in lysates of PC12 cells the endogenous TRP-6 protein was detected by Western blot analysis. It is concluded that PC12 cells express a diacylglycerol-activated, non-selective cation channel. Expression of this channel function correlates with expression of the TRP-3 and TRP-6 proteins, which have been shown previously to be activated by diacylglycerol when expressed heterologously in animal cells [Hofmann, Obukhov, Schaefer, Harteneck, Gudermann, and Schultz (1999) Nature (London) 397, 259-263].

L1 ANSWER 9 OF 19 MEDLINE on STN

AN 2001469045 MEDLINE

DN 21405054 PubMed ID: 11513973

TI Maitotoxin activates an endogenous non-selective cation channel and is an effective initiator of the activation of the heterologously expressed hTRPC-1 (transient receptor potential) non-selective cation channel in H4-IIIE liver cells.

AU Brereton H M; Chen J; Rychkov G; Harland M L; Barritt G J

CS Department of Medical Biochemistry, School of Medicine, Flinders University, Adelaide, SA, Australia.

SO BIOCHIMICA ET BIOPHYSICA ACTA, (2001 Aug 22) 1540 (2) 107-26.  
Journal code: 0217513. ISSN: 0006-3002.

CY Netherlands

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200109

ED Entered STN: 20010830  
Last Updated on STN: 20010924

Entered Medline: 20010920

AB The structures and mechanisms of activation of non-selective cation channels (NSCCs) are not well understood although NSCCs play important roles in the regulation of metabolism, ion transport, cell volume and cell shape. It has been proposed that TRP (**transient receptor potential**) proteins are the molecular correlates of some NSCCs. Using fura-2 and patch-clamp recording, it was shown that the maitotoxin-activated cation channels in the H4-IIE rat liver cell line admit  $\text{Ca}^{2+}$ ,  $\text{Mn}^{2+}$  and  $\text{Na}^{+}$ , have a high selectivity for  $\text{Na}^{+}$  compared with  $\text{Ca}^{2+}$ , and are inhibited by  $\text{Gd}^{3+}$  (half-maximal inhibition at 1  $\mu\text{M}$ ). Activation of the channels by maitotoxin was inhibited by increasing the extracellular  $\text{Ca}^{2+}$  concentration or by inclusion of 10 mM EGTA in the patch pipette. mRNA encoding TRP proteins 1, 2 and 3 at levels comparable with those in brain was detected using reverse transcriptase-polymerase chain reaction in poly(A)(+) RNA prepared from H4-IIE cells and freshly-isolated rat hepatocytes. In H4-IIE cells transiently transfected with cDNA encoding hTRPC-1, the expressed hTRPC-1 protein was chiefly located at intracellular sites and at the plasma membrane. Cells expressing hTRPC-1 exhibited a substantial enhancement of maitotoxin-initiated  $\text{Ca}^{2+}$  inflow and a modest enhancement of thapsigargin-initiated  $\text{Ca}^{2+}$  inflow (measured using fura-2) and no enhancement of the highly  $\text{Ca}^{2+}$ -selective store-operated  $\text{Ca}^{2+}$  current (measured using patch-clamp recording). In cells expressing hTRPC-1, maitotoxin activated channels which were not found in untransfected cells, have an approximately equal selectivity for  $\text{Na}^{+}$  and  $\text{Ca}^{2+}$ , and are inhibited by  $\text{Gd}^{3+}$  (half-maximal inhibition at 3  $\mu\text{M}$ ). It is concluded that in liver cells (i) maitotoxin initiates the activation of endogenous NSCCs with a high selectivity for  $\text{Na}^{+}$  compared with  $\text{Ca}^{2+}$ ; (ii) TRP proteins 1, 2 and 3 are expressed; (iii) maitotoxin is an effective initiator of activation of heterologously expressed hTRPC-1 channels; and (iv) the endogenous TRP-1 protein is unlikely to be the molecular counterpart of the maitotoxin-activated NSCCs nor the highly  $\text{Ca}^{2+}$ -selective store-operated  $\text{Ca}^{2+}$  channels.

L1 ANSWER 10 OF 19 MEDLINE on STN

AN 2001386794 MEDLINE

DN 21334158 PubMed ID: 11440466

TI Recent developments in non-excitabile cell calcium entry.

AU Elliott A C

CS School of Biological Sciences, University of Manchester, Manchester, UK..  
acelliot@maill.mcc.ac.uk

SO CELL CALCIUM, (2001 Aug) 30 (2) 73-93. Ref: 151

Journal code: 8006226. ISSN: 0143-4160.

CY Scotland: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, ACADEMIC)

LA English

FS Priority Journals

EM 200109

ED Entered STN: 20011001

Last Updated on STN: 20011001

Entered Medline: 20010927

AB Influx of calcium into cells following stimulation of cell surface receptors is a key process controlling cellular activity. However, despite intensive research, there is still no consensus on precisely how calcium entry is controlled in electrically non-excitable cells. In particular, the regulation of depletion-activated or 'capacitative' calcium entry continues to be a focus of debate. Work published in the last 2 years has lent new impetus to the so-called 'conformational coupling' theory, although evidence for the existence of soluble messengers between the ER and the plasma membrane also continues to

appear. In addition, there remains disagreement on whether intra-store  $[Ca(2+)]$  has to fall below a threshold before  $Ca(2+)$  entry is activated. A further major question is the identity of the putative depletion-operated  $Ca(2+)$  channel or channels. Here discussion has largely focussed on whether homologue(s) of the *Drosophila* TRP ('**Transient Receptor Potential**') protein is/are the elusive channel, or at least a part of it. Finally, it remains possible that  $Ca(2+)$  entry mechanisms other than depletion-activated channels may be important in agonist-evoked  $Ca(2+)$  influx. This commentary summarizes recent developments in the field, and highlights both current debates and critical unsolved questions.  
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L1 ANSWER 11 OF 19 MEDLINE on STN  
AN 2001363427 MEDLINE  
DN 21317769 PubMed ID: 11207380  
TI **Transient receptor potential protein**  
mRNA expression in rat substantia nigra.  
AU Sylvester J B; Mwanjewe J; Grover A K  
CS Department of Biology, McMaster University, Hamilton, Ontario, Canada.  
SO NEUROSCIENCE LETTERS, (2001 Mar 9) 300 (2) 83-6.  
Journal code: 7600130. ISSN: 0304-3940.  
CY Ireland  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200108  
ED Entered STN: 20010813  
Last Updated on STN: 20010813  
Entered Medline: 20010809  
AB Receptor gated  $Ca^{2+}$  entry has been associated with transient receptor potential (TRP) proteins encoded by several different genes. Here, we compare expression of mRNA for TRP isoforms encoded by genes TRP1-6 in the rat substantia nigra and whole brain. The substantia nigra and the whole brain expressed mRNA predominantly for TRP3 and TRP6. The levels of TRP1, 2, 4 and 5 were very low in both. The TRP6 mRNA levels in substantia nigra and the whole brain were comparable while those for TRP3 were significantly lower in substantia nigra than in the whole brain. Thus substantia nigra differs from the whole brain in its TRP expression.

L1 ANSWER 12 OF 19 MEDLINE on STN  
AN 2001226349 MEDLINE  
DN 21113398 PubMed ID: 11179201  
TI The **transient receptor potential protein** homologue TRP6 is the essential component of vascular  $\alpha(1)$ -adrenoceptor-activated  $Ca(2+)$ -permeable cation channel.  
CM Comment in: Circ Res. 2001 Feb 16;88(3):256-9  
AU Inoue R; Okada T; Onoue H; Hara Y; Shimizu S; Naitoh S; Ito Y; Mori Y  
CS Department of Pharmacology, Graduate School of Medical Sciences, Kyushu University, Fukuoka.. inouery@pharmaco.med.kyushu-u.ac.jp  
SO CIRCULATION RESEARCH, (2001 Feb 16) 88 (3) 325-32.  
Journal code: 0047103. ISSN: 1524-4571.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200104  
ED Entered STN: 20010502  
Last Updated on STN: 20010521  
Entered Medline: 20010426  
AB The *DROSOPHILA*: **transient receptor potential protein** (TRP) and its mammalian homologues are thought to be

Ca(2+)-permeable cation channels activated by G protein (G(q/11))-coupled receptors and are regarded as an interesting molecular model for the Ca(2+) entry mechanisms associated with stimulated phosphoinositide turnover and store depletion. However, there is little unequivocal evidence linking mammalian TRPs with particular native functions. In this study, we have found that heterologous expression of murine TRP6 in HEK293 cells reproduces almost exactly the essential biophysical and pharmacological properties of alpha(1)-adrenoceptor-activated nonselective cation channels (alpha(1)-AR-NSCC) previously identified in rabbit portal vein smooth muscle. Such properties include activation by diacylglycerol; S-shaped current-voltage relationship; high divalent cation permeability; unitary conductance of 25 to 30 pS and augmentation by flufenamate and Ca(2+); and blockade by Cd(2+), La(3+), Gd(3+), SKF96365, and amiloride. Reverse transcriptase-polymerase chain reaction and confocal laser scanning microscopy using TRP6-specific primers and antisera revealed that the level of TRP6 mRNA expression was remarkably high in both murine and rabbit portal vein smooth muscles as compared with other TRP subtypes, and the immunoreactivity to TRP6 protein was localized near the sarcolemmal region of single rabbit portal vein myocytes. Furthermore, treatment of primary cultured portal vein myocytes with TRP6 antisense oligonucleotides resulted in marked inhibition of TRP6 protein immunoreactivity as well as selective suppression of alpha(1)-adrenoceptor-activated, store depletion-independent cation current and Ba(2+) influx. These results strongly indicate that TRP6 is the essential component of the alpha(1)-AR-NSCC, which may serve as a store depletion-independent Ca(2+) entry pathway during increased sympathetic activity.

L1 ANSWER 13 OF 19 MEDLINE on STN

AN 2001148003 MEDLINE

DN 21099836 PubMed ID: 11163362

TI Alternative splice variants of hTrp4 differentially interact with the C-terminal portion of the inositol 1,4,5-trisphosphate receptors.

AU Mery L; Magnino F; Schmidt K; Krause K H; Dufour J F

CS Division of Infectious Diseases, Geneva University Hospital, Switzerland.

SO FEBS LETTERS, (2001 Jan 5) 487 (3) 377-83.

Journal code: 0155157. ISSN: 0014-5793.

CY Netherlands

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200103

ED Entered STN: 20010404

Last Updated on STN: 20010404

Entered Medline: 20010315

AB The molecular basis of capacitative (or store-operated) Ca2+ entry is still subject to debate. The **transient receptor**

**potential proteins** have been hypothesized to be structural components of store-operated Ca2+ channels and recent evidence suggests that Trp3 and its closely related homolog Trp6 are gated by the N-terminal region of the inositol 1,4,5-trisphosphate receptors (InsP3R). In this study, we report the existence of two isoforms of the human Trp4 protein, referred to as alpha-hTrp4 and beta-hTrp4. The shorter variant beta-hTrp4 is generated through alternative splicing and lacks the C-terminal amino acids G785-S868. Using a yeast two-hybrid assay and glutathione-S-transferase-pulldown experiments, we found that the C-terminus of alpha-hTrp4, but not of beta-hTrp4, associates in vitro with the C-terminal domain of the InsP(3) receptors type 1, 2 and 3. Thus, we describe a novel interaction between Trp proteins and InsP3R and we provide evidence suggesting that the formation of hTrp4-InsP3R complexes may be regulated by alternative splicing.

L1 ANSWER 14 OF 19 MEDLINE on STN

AN 2001082647 MEDLINE  
 DN 20538370 PubMed ID: 10980191  
 TI Expression of truncated **transient receptor potential protein** lalpha (Trplalpha ): evidence that the Trp1 C terminus modulates store-operated Ca<sup>2+</sup> entry.  
 AU Singh B B; Liu X; Ambudkar I S  
 CS Secretory Physiology Section, Gene Therapy and Therapeutics Branch, NIDCR, National Institutes of Health, Bethesda, Maryland 20892, USA.  
 SO JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Nov 24) 275 (47) 36483-6.  
 Journal code: 2985121R. ISSN: 0021-9258.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 200101  
 ED Entered STN: 20010322  
 Last Updated on STN: 20010322  
 Entered Medline: 20010108  
 AB **Transient receptor potential protein** 1 (Trp1) has been proposed as a component of the store-operated Ca(2+) entry (SOCE) channel. However, the exact mechanism by which Trp1 is regulated by store depletion is not known. Here, we examined the role of the Trp1 C-terminal domain in SOCE by expressing hTrplalpha lacking amino acids 664-793 (DeltaTrplalpha) or full-length hTrplalpha in the HSG (human submandibular gland) cell line. Both carbachol (CCh) and thapsigargin (Tg) activated sustained Ca(2+) influx in control (nontransfected), DeltaTrplalpha-, and Trplalpha-expressing cells. Sustained [Ca(2+)](i), following stimulation with either Tg or CCh in DeltaTrplalpha-expressing cells, was about 1.5-2-fold higher than in Trplalpha-expressing cells and 4-fold higher than in control cells. Importantly, (i) basal Ca(2+) influx and (ii) Tg- or CCh-stimulated internal Ca(2+) release were similar in all the cells. A similar increase in Tg-stimulated Ca(2+) influx was seen in cells expressing Delta2Trplalpha, lacking the C-terminal domain amino acid 649-793, which includes the EWKFAR sequence. Further, both inositol 1,4,5-trisphosphate receptor-3 and caveolin-1 were immunoprecipitated with DeltaTrplalpha and Trplalpha. In aggregate, these data suggest that (i) the EWKFAR sequence does not contribute significantly to the Trp1-associated increase in SOCE, and (ii) the Trp1 C-terminal region, amino acids 664-793, is involved in the modulation of SOCE.

L1 ANSWER 15 OF 19 MEDLINE on STN  
 AN 2000472607 MEDLINE  
 DN 20381044 PubMed ID: 10920270  
 TI Store depletion by caffeine/ryanodine activates capacitative Ca(2+) entry in nonexcitable A549 cells.  
 AU Xue H H; Zhao D M; Suda T; Uchida C; Oda T; Chida K; Ichiyama A; Nakamura H  
 CS First Department of Biochemistry, and Second Division, Department of Internal Medicine, Hamamatsu University School of Medicine, Handa-cho, Hamamatsu, Shizuoka 431-3192, Japan.. xueh@nhlbi.nih.gov  
 SO JOURNAL OF BIOCHEMISTRY, (2000 Aug) 128 (2) 329-36.  
 Journal code: 0376600. ISSN: 0021-924X.  
 CY Japan  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 200010  
 ED Entered STN: 20001012  
 Last Updated on STN: 20001012  
 Entered Medline: 20001003  
 AB Capacitative Ca(2+) entry is essential for refilling intracellular Ca(2+) stores and is thought to be regulated primarily by inositol 1,

4,5-trisphosphate (IP(3))-sensitive stores in nonexcitable cells. In nonexcitable A549 cells, the application of caffeine or ryanodine induces Ca(2+) release in the absence of extracellular Ca(2+) similar to that induced by thapsigargin (Tg), and Ca(2+) entry occurs upon the readdition of extracellular Ca(2+). The channels thus activated are also permeable to Mn(2+). The channels responsible for this effect appear to be activated by the depletion of caffeine/ryanodine-sensitive stores per se, as evidenced by the activation even in the absence of increased intracellular Ca(2+) concentration. Tg pretreatment abrogates the response to caffeine/ryanodine, whereas Tg application subsequent to caffeine/ryanodine treatment induces further Ca(2+) release. The response to caffeine/ryanodine is also abolished by initial ATP application, whereas ATP added subsequent to caffeine/ryanodine induces additional Ca(2+) release. RT-PCR analyses showed the expression of a type 1 ryanodine receptor, two human homologues of **transient receptor potential protein** (hTrp1 and hTrp6), as well as all three types of the IP(3) receptor. These results suggest that in A549 cells, (i) capacitative Ca(2+) entry can also be regulated by caffeine/ryanodine-sensitive stores, and (ii) the RyR-gated stores interact functionally with those sensitive to IP(3), probably via Ca(2+)-induced Ca(2+) release.

L1 ANSWER 16 OF 19 MEDLINE on STN  
AN 2000412541 MEDLINE  
DN 20366135 PubMed ID: 10903843  
TI Mtr1, a novel biallelically expressed gene in the center of the mouse distal chromosome 7 imprinting cluster, is a member of the Trp gene family.  
AU Enklaar T; Esswein M; Oswald M; Hilbert K; Winterpacht A; Higgins M; Zabel B; Prawitt D  
CS Children's Hospital, University of Mainz, Langenbeckstrasse 1, Mainz, D-55101, Germany.. enklaar@wserv.kinder.klinik.uni-mainz.de  
NC CA63333 (NCI)  
SO GENOMICS, (2000 Jul 15) 67 (2) 179-87.  
Journal code: 8800135. ISSN: 0888-7543.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200008  
ED Entered STN: 20000907  
Last Updated on STN: 20000907  
Entered Medline: 20000829  
AB We recently described a novel putative Ca(2+) channel gene, MTR1, which shows a high level of homology to the human TRPC7 gene and the melastatin 1 (MLSN1) gene, another Trp (**transient receptor potential protein**)-related gene whose transcript was found to be downregulated in metastatic melanomas. It maps to human chromosome band 11p15.5, which is associated with the Beckwith-Wiedemann syndrome and predisposition to a variety of neoplasias. Here we report the isolation and characterization of the murine orthologue Mtr1. The chromosomal localization on distal chromosome 7 places it in a cluster of imprinted genes, flanked by the previously described Tapal and Kcnql genes. The Mtr1 gene encodes a 4.4-kb transcript, present in a variety of fetal and adult tissues. The putative open reading frame consists of 24 exons, encoding 1158 amino acids. Transmembrane prediction algorithms indicate the presence of six membrane-spanning domains in the proposed protein. Imprinting analysis, using RT-PCR on RNA from reciprocal mouse crosses harboring a sequence polymorphism, revealed biallelic expression of Mtr1 transcripts at all stages and tissues examined.  
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L1 ANSWER 17 OF 19 MEDLINE on STN  
 AN 1999419008 MEDLINE  
 DN 99419008 PubMed ID: 10488066  
 TI Molecular and functional characterization of a novel mouse  
**transient receptor potential protein**  
 homologue TRP7. Ca(2+)-permeable cation channel that is constitutively  
 activated and enhanced by stimulation of G protein-coupled receptor.  
 AU Okada T; Inoue R; Yamazaki K; Maeda A; Kurosaki T; Yamakuni T; Tanaka I;  
 Shimizu S; Ikenaka K; Imoto K; Mori Y  
 CS Laboratory of Humoral Information, Department of Information Physiology,  
 National Institute for Physiological Sciences, Okazaki 444-8585, Japan.  
 SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Sep 24) 274 (39) 27359-70.  
 Journal code: 2985121R. ISSN: 0021-9258.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 OS GENBANK-AF139923  
 EM 199911  
 ED Entered STN: 20000111  
 Last Updated on STN: 20000111  
 Entered Medline: 19991104  
 AB Characterization of mammalian homologues of *Drosophila* **transient**  
**receptor potential protein** (TRP) is an  
 important clue to understand molecular mechanisms underlying Ca(2+) influx  
 activated in response to stimulation of G(q) protein-coupled receptors in  
 vertebrate cells. Here we have isolated cDNA encoding a novel seventh  
 mammalian TRP homologue, TRP7, from mouse brain. TRP7 showed abundant RNA  
 expression in the heart, lung, and eye and moderate expression in the  
 brain, spleen, and testis. TRP7 recombinantly expressed in human  
 embryonic kidney cells exhibited distinctive functional features, compared  
 with other TRP homologues. Basal influx activity accompanied by reduction  
 in Ca(2+) release from internal stores was characteristic of  
 TRP7-expressing cells but was by far less significant in cells expressing  
 TRP3, which is structurally the closest to TRP7 in the TRP family. TRP7  
 induced Ca(2+) influx in response to ATP receptor stimulation at ATP  
 concentrations lower than those necessary for activation of TRP3 and for  
 Ca(2+) release from the intracellular store, which suggests that the TRP7  
 channel is activated independently of Ca(2+) release. In fact, TRP7  
 expression did not affect capacitative Ca(2+) entry induced by  
 thapsigargin, whereas TRP7 greatly potentiated Mn(2+) influx induced by  
 diacylglycerols without involvement of protein kinase C.  
 Nystatin-perforated and conventional whole-cell patch clamp recordings  
 from TRP7-expressing cells demonstrated the constitutively activated and  
 ATP-enhanced inward cation currents, both of which were initially blocked  
 and then subsequently facilitated by extracellular Ca(2+) at a  
 physiological concentration. Impairment of TRP7 currents by internal  
 perfusion of the Ca(2+) chelator 1,2-bis(2-aminophenoxy)ethane-N,N,N',N'-  
 tetraacetic acid revealed an essential role of intracellular Ca(2+) in  
 activation of TRP7, and their potent activation by the diacylglycerol  
 analogue suggests that the TRP7 channel is a new member of  
 diacylglycerol-activated cation channels. Relative permeabilities  
 indicate that TRP7 is slightly selective to divalent cations. Thus, our  
 findings reveal an interesting correspondence of TRP7 to the background  
 and receptor stimulation-induced cation currents in various native  
 systems.

L1 ANSWER 18 OF 19 MEDLINE on STN  
 AN 1999306853 MEDLINE  
 DN 99306853 PubMed ID: 10377243  
 TI Stimulation of *Drosophila* TrpL by capacitative Ca2+ entry.  
 AU Estacion M; Sinkins W G; Schilling W P

CS Rammelkamp Center for Education and Research, MetroHealth Medical Center,  
and Department of Physiology and Biophysics, Case Western Reserve  
University School of Medicine, 2500 MetroHealth Drive, Cleveland, OH  
44109-1998, USA.

NC GM52019 (NIGMS)

SO BIOCHEMICAL JOURNAL, (1999 Jul 1) 341 ( Pt 1) 41-9.  
Journal code: 2984726R. ISSN: 0264-6021.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199909

ED Entered STN: 19990925  
Last Updated on STN: 19990925  
Entered Medline: 19990903

AB Trp-like protein (TrpL, where Trp is **transient receptor**  
**-potential protein**) of Drosophila, a non-selective  
cation channel activated in photoreceptor cells by a phospholipase  
C-dependent mechanism, is thought to be a prototypical receptor-activated  
channel. Our previous studies showed that TrpL channels are not activated  
by depletion of internal Ca<sup>2+</sup> stores when expressed in Sf9 cells. Using  
fura-2 to measure cation influx via TrpL, and cell-attached patch  
recordings to monitor TrpL single-channel activity directly, we have found  
a thapsigargin-induced increase in TrpL activity in the presence of  
extracellular bivalent cations, with Ca<sup>2+</sup>>Sr<sup>2+</sup>>> Ba<sup>2+</sup>. The increase in  
TrpL channel activity was blocked by concentrations of La<sup>3+</sup> that  
completely inhibited endogenous capacitative Ca<sup>2+</sup> entry (CCE), but have no  
effect on TrpL, suggesting that TrpL exhibits trans-stimulation by cation  
entry via CCE. TrpL has two putative calmodulin (CaM)-binding domains,  
designated CBS-1 and CBS-2. To determine which site may be required for  
stimulation of TrpL by the cytosolic free Ca<sup>2+</sup> concentration ([Ca<sup>2+</sup>]<sub>i</sub>), a  
chimaeric construct was created in which the C-terminal domain of TrpL  
containing CBS-2 was attached to human TrpC1, a short homologue of Trp  
that is not activated by depletion of internal Ca<sup>2+</sup> stores or by a rise in  
[Ca<sup>2+</sup>]<sub>i</sub>. This gain-of-function mutant, designated TrpC1-TrpL, exhibited  
trans-stimulation by Ca<sup>2+</sup> entry via CCE. Examination of CaM binding in  
gel-overlay experiments showed that TrpL and the TrpC1-TrpL chimaera bound  
CaM, but TrpC1 or a truncated version of TrpL lacking CBS-2 did not.  
These results suggest that only CBS-2 binds CaM in native TrpL and that  
the C-terminal domain containing this site is important for  
trans-stimulation of TrpL by CCE.

L1 ANSWER 19 OF 19 MEDLINE on STN

AN 97157494 MEDLINE

DN 97157494 PubMed ID: 9003779

TI **The transient receptor potential**  
**protein** (Trp), a putative store-operated Ca<sup>2+</sup> channel essential  
for phosphoinositide-mediated photoreception, forms a signaling complex  
with NorpA, InaC and InaD.

AU Huber A; Sander P; Gobert A; Bahner M; Hermann R; Paulsen R

CS Zoological Institute I, University of Karlsruhe, Germany.

SO EMBO JOURNAL, (1996 Dec 16) 15 (24) 7036-45.  
Journal code: 8208664. ISSN: 0261-4189.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

OS GENBANK-Z80230

EM 199702

ED Entered STN: 19970227  
Last Updated on STN: 19980206  
Entered Medline: 19970213



AB    **The transient receptor potential**

**protein** (Trp) is a putative capacitative  $\text{Ca}^{2+}$  entry channel present in fly photoreceptors, which use the inositol 1,4,5-trisphosphate (InsP3) signaling pathway for phototransduction. By immunoprecipitation studies, we find that Trp is associated into a multiprotein complex with the norpA-encoded phospholipase C, an eye-specific protein kinase C (InaC) and with the InaD protein (InaD). InaD is a putative substrate of InaC and contains two PDZ repeats, putative protein-protein interaction domains. These proteins are present in the photoreceptor membrane at about equimolar ratios. The Trp homolog analyzed here is isolated together with NorpA, InaC and InaD from blowfly (*Calliphora*) photoreceptors. Compared to *Drosophila* Trp, the *Calliphora* Trp homolog displays 77% amino acid identity. The highest sequence conservation is found in the region that contains the putative transmembrane domains S1-S6 (91% amino acid identity). As investigated by immunogold labeling with specific antibodies directed against Trp and InaD, the Trp signaling complex is located in the microvillar membranes of the photoreceptor cells. The spatial distribution of the signaling complex argues against a direct conformational coupling of Trp to an InsP3 receptor supposed to be present in the membrane of internal photoreceptor  $\text{Ca}^{2+}$  stores. It is suggested that the organization of signal transducing proteins into a multiprotein complex provides the structural basis for an efficient and fast activation and regulation of  $\text{Ca}^{2+}$  entry through the Trp channel.